

We Claim:

1. A device for recording electrical activity of a biological tissue slice which comprises:
a chamber having a wall and a bottom defining a chamber interior volume that will
5 hold liquid and being open at the top with an upper edge defining the opening,
a stimulating electrode wire and a recording electrode wire, which are both rigid and
fixable at a position extending into the chamber interior volume so that the electrode ends are
at a chosen position within the volume, both electrode wires also extending outside the
chamber to electrical stimulating and recording devices, respectively,

10 a cap with a protrusion, the cap having a capping part corresponding to at least part of
upper edge defining the opening of the chamber so that it can be placed over the chamber
opening in a defined capped position, the protrusion being part of or connected to the cap
such that, when the cap is placed over the chamber opening in its defined position, the
protrusion extends a fixed distance into chamber interior volume, and

15 a liquid-permeable and flexible bottom net material provided across at least part of a
horizontal cross section of the chamber interior volume for holding a biological tissue slice
within the chamber interior volume,

wherein the extending of the protrusion a fixed distance into the chamber interior
volume and the fixing of the electrode wires so that the electrode ends are at a chosen
20 position within the chamber interior volume are such that, when the cap is in its defined
capped position and the bottom net material is holding a biological tissue slice, the movement
of the protrusion into the chamber interior volume results in penetration of the electrode ends
into the interior of the biological tissue slice.

25 2. The device of claim 1, wherein:

the cap is open to the exterior above the protrusion,

the protrusion is hollow with openings at the top and bottom such that the interior
chamber volume is open to the top through the protrusion and cap,

30 a liquid-permeable and flexible top net material is provided across at least part of a
horizontal cross section of the chamber interior volume above the bottom net material and
across at least part of a horizontal cross section of the bottom opening of the protrusion,

wherein, when the cap is in its defined position and the bottom net material is holding
a biological tissue slice, the outline of the bottom of the protrusion circumscribes but does not
touch the tissue slice, the top net material contacts the top of the biological tissue slice and

the movement of the protrusion pushes the top and bottom net materials and the biological tissue slice down onto the ends of the electrodes so that they penetrate through the bottom net material into the interior of the biological tissue slice.

3. The device of claim 2, wherein the top net material is provided across the bottom opening of the protrusion or just inside the bottom opening of the protrusion.

4. The device of claim 1, wherein:

the bottom of the chamber interior volume has a bottom through hole extending down to the exterior,

the device further comprises a plug which can be inserted into the bottom through hole such that, optionally with the use of a sealer material, the plug provides at least part of the bottom of the chamber interior volume so that it will hold liquid,

the plug is adjustable as to its extent of insertion into the bottom through hole and a means for holding the plug in a selected position is provided, and

the plug holds the electrode wires so that they extend from outside the chamber, through the bottom through hole and into the chamber interior volume to their fixable position extending upward into the chamber interior which is adjustable by adjusting the extent of insertion of the plug.

5. The device of claim 4, wherein the means for holding the plug in a selected position is provided by a screw threaded through the chamber wall and into the bottom through hole to contact and hold in place the plug inserted therein.

6. The device of claim 4, wherein the electrode wires are attached to the outside wall of the plug, the electrode wires run inside the plug and out the top or the electrode wires run inside a slot in the outside wall of the plug.

7. The device of claim 2, wherein:

the bottom of the chamber interior volume has a bottom through hole extending down to the exterior,

the device further comprises a plug which can be inserted into the bottom through hole such that, optionally with the use of a sealer material, the plug provides at least part of the bottom of the chamber interior volume so that it will hold liquid,

the plug is adjustable as to its extent of insertion into the bottom through hole and a means for holding the plug in a selected position is provided, and

the plug holds the electrode wires so that they extend from outside the chamber, through the bottom through hole and into the chamber interior volume to the their fixable position extending upward into the chamber interior which is adjustable by adjusting the extent of insertion of the plug.

8. The device of claim 7, wherein the means for holding the plug in a selected position is provided by a screw threaded through the chamber wall and into the bottom through hole to contact and hold in place the plug inserted therein.

9. The device of claim 7, wherein the electrode wires are attached to the outside wall of the plug, the electrode wires run inside the plug and out the top or the electrode wires run inside a slot in the outside wall of the plug.

10. The device of claim 2, which additionally comprises a light source providing light directed up from below and into the chamber interior volume such that, when the device is capped and a biological tissue slice is contained, shadows of the electrode wire ends can be seen through the biological tissue slice when viewed from above through the open cap and protrusion.

11. The device of claim 7, which additionally comprises a light source providing light directed up from the plug, which is transparent at the top, and into the chamber interior volume such that, when the device is capped and a biological tissue slice is contained, shadows of the electrode wire ends can be seen through the biological tissue slice when viewed from above through the open cap and protrusion.

12. The device of claim 11, wherein the light is provided by an LED within the plug and the plug is transparent at the top.

13. The device of claim 11, wherein the plug comprises one or more concave or flat lenses at the top for directing the light.

14. The device of claim 1, which further comprises an inlet and outlet to the chamber interior volume for continuous flow of a perfusion liquid therethrough.
15. The device of claim 2, which further comprises an inlet and outlet to the chamber interior volume for continuous flow of a perfusion liquid therethrough and the protrusion contains openings in its walls to allow perfusion into the interior of the hollow protrusion.
16. The device of claim 1, wherein the chamber interior volume has a top portion of larger horizontal cross section which receives the cap and a bottom portion of smaller horizontal cross section which contains the bottom net material and receives the protrusion.
17. The device of claim 16, wherein the chamber exterior, the top and bottom portions of the chamber interior volume and the cap and protrusion all have circular horizontal cross sections.
18. The device of claim 16, wherein the chamber exterior, the top and bottom portions of the chamber interior volume and the cap and protrusion all have square horizontal cross sections.
19. The device of claim 1, wherein:
the chamber has an external profile, horizontally, of 300 - 5000 mm², the profile is essentially constant along the height of the chamber and the chamber has a height of 20 - 100 mm, and
the interior volume of the chamber has a horizontal cross section of about 75 - 500 mm² and a depth of about 5-20 mm.
20. The device of claim 1, wherein the electrode wires are of a conductive metal wire material with a thickness of 10 - 50 μm.
21. The device of claim 20, wherein the electrode wires are non-oxidizing platinum, platinum/iridium or tungsten wire electrodes, partially coated with a non-stick material.
22. The device of claim 1, wherein the electrodes are fixable in a position about 50-500 μm below the bottom net when the cap is not in place, the electrode wires extend from the

bottom of the chamber interior towards the top of the chamber parallel to each other or slightly diagonally toward each other, and the ends of the stimulating and recording electrode wires are spaced apart from 20 - 500 μm from each other.

5 **23.** The device of claim 1, wherein the cap and protrusion are an integral piece.

10 **24.** The device of claim 2, wherein the protrusion has a circular horizontal cross section and the top net material is provided in the bottom of the protrusion opening by a net material stretched over a metal or plastic ring of a diameter corresponding to the protrusion interior which ring is wedged or affixed into the protrusion interior.

15 **25.** The device of claim 1, wherein the bottom of the chamber interior volume has a circular horizontal cross section and the bottom net material is provided across the chamber interior volume by a net material stretched over a metal or plastic ring of a diameter corresponding to the bottom of the chamber interior volume which ring is wedged or affixed into the bottom of the chamber interior volume.

20 **26.** The device of claim 2, wherein the top and bottom net material are of a polymer mesh material.

27. The device of claim 1, wherein the bottom net material is about 1 - 10 mm above the bottom of the chamber interior.

25 **28.** The device of claim 1, wherein the protrusion is provided so that, when in capped position, the protrusion pushes the bottom net down at least 50 μm and up to 350 μm .

30 **29.** A system for recording electrical activity of multiple biological tissue slices which comprises two or more devices according to claim 1 provided together on a vibration/isolation table.

30. A system for recording electrical activity of multiple biological tissue slices which comprises ten to twenty devices according to claim 1 provided together on a vibration/isolation table.

31. A system for recording electrical activity of multiple biological tissue slices which comprises sixteen devices according to claim 1 provided together on a vibration/isolation table.
32. A method for measuring the electrical excitability properties or potential of a small, thin sample of biological tissue using the device of claim 1, which comprises:
placing the sample on the bottom net material positioned above the top ends of the stimulating electrode wire and recording electrode wire,
providing the chamber interior volume with a perfusion liquid either before or after placing the sample,
placing the cap with protrusion in its defined capped position such that the movement of the protrusion into the chamber interior volume pushes the bottom net material and biological tissue slice down onto the ends of the electrode wires so that they penetrate through the bottom net material into the interior of the biological tissue slice,
optionally, providing a stimulating electrical activity through the stimulating electrode wire, and
recording the electrical activity of the sample through the recording electrode wire.
33. The method of claim 32, wherein the biological tissue is brain tissue or spinal cord tissue slices.
34. The method of claim 32, wherein the biological tissue is mammalian hippocampal brain tissue slices.
35. The method of claim 32, wherein the biological tissue is a tissue slice having a thickness of from 200 - 500 μm .
36. The method of claim 32, wherein the method records long term potentiation (LTP) of a brain slice sample.
37. The method of claim 32, which further comprises contacting the biological tissue with a test compound before and/or during recording of electrical activity to assess the effect of the test compound on the electrical activity of the biological tissue.

38. The method of claim 37, wherein the method records long term potentiation (LTP) of a brain slice sample.
39. The method of claim 38, wherein the brain slice sample is a rat hippocampal brain slice.
40. The method of claim 38, wherein the test compound is mixed with the perfusion fluid for contacting the sample.
41. The method of claim 40, wherein the test compound is provided at a concentration of from 1 nanomolar (nM) to 50 micromolar (μ M).
42. The method of claim 40, wherein multiple, essentially identical chambers, are used to conduct parallel runs of samples at differing concentrations of test compound.
43. The method of claim 38, wherein the LTP is assessed of a sample without test compound and with test compound to assess the effect of the test compound on the LTP.
44. The method of claim 32, wherein a stimulating activity through the stimulating electrode wire is provided as about a 40 Hz theta burst tetanization.
45. The method of claim 38, wherein a stimulating activity through the stimulating electrode wire is provided as about a 40 Hz theta burst tetanization.
46. The method of claim 32, wherein a stimulating electrical activity of at least 50% of the maximum response is provided through the stimulating electrode wire.
47. The method of claim 38, wherein a stimulating electrical activity of at least 50% of the maximum response is provided through the stimulating electrode wire.
48. The method of claim 32, wherein the distance between the stimulating electrode wire end and the recording electrode wire end is less than 200 μ m.

49. The method of claim 32, wherein stimulating electrical activity under a tetanizing protocol is provided through the stimulating electrode wire.

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